

APPLICANT'S REMARKS

1. Status of the Claims

Claims 1, 3–7, 10–12, 19, 21, and 22 are pending. Claims 1 and 10 are currently amended.

Claims 2, 8, 9, 13–18, and 20 are canceled. Claims 21 and 22 are new.

2. Rejection of Claims Under 35 U.S.C. 103(a) Based on DOMINGUES in view of WYLLIE and further in view of APELER, GELLER, BONSCH, or THØGERSEN

Claims 1–6, 8, 11, 13, 14, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over DOMINGUES in view of WYLLIE.

The Examiner asserts that DOMINGUES teaches the presently claimed invention, but for the step of separating the denatured IL-4 or muteins thereof using an immobilized metal chelate affinity chromatography (IMAC) system. The Examiner references WYLLIE for “a method for purifying a protein containing histidine residues using immobilizing metal affinity chromatography.” The Examiner concluded that it would have been obvious for one of ordinary skill in the art to modify the process of DOMINGUES with the IMAC method of WYLLIE because IMAC “provides an alternative approach for purifying IL-4...”

The Examiner further relies on APELER for expression of IL-4 R121D Y124D as recited in claim 7; GELLER for artificial chaperones, such as β -cyclodextrin, as recited in claims 9 and 10; BONSCH for expression of mIL-4 Q116D or Y119D as recited in claim 12; and THØGERSEN

for renaturing the denatured IL-4 or muteins thereof prior to releasing the IL-4 or muteins thereof from the IMAC system, as recited in claim 20.

3. Applicant Requests Reconsideration and Withdrawn of the Rejections

The Applicant respectfully disagrees with the Examiner and submits that the present claims are not obvious based on DOMINGUES in view of WYLLIE and further in view of APELER, GELLER, BONSCH, or THØGERSEN. In particular, the cited references, considered as a whole, do not establish that one skilled in the art at the time of the invention would predict that guanidine-denatured IL-4 (or a mutein thereof) would successfully bind to IMAC-resins.

4. The Legal Test for Obviousness

The Supreme Court recently addressed the issue of obviousness in KSR International Co. v. Teleflex Inc., 127 S. Ct. 1727 (2007). The Court stated that the Graham v. John Deere Co. of Kansas City, 383 U.S. 1 (1966), factors still control an obviousness inquiry. Those factors are: 1) “the scope and content of the prior art”; 2) the “differences between the prior art and the claims”; 3) “the level of ordinary skill in the pertinent art”; and 4) objective evidence of nonobviousness. KSR, 127 S. Ct. at 1734 (quoting Graham, 383 U.S. at 17–18).

5. The Evidence Does Not Establish That One Skilled in The Art at the Time Of The Invention Would Predict That Guanidine-Denatured IL-4 (Or A Mutein Thereof) Would Bind To IMAC-Resins

Considering the cited references as a whole, the Applicant respectfully submits that the evidence of record does not establish that one skilled in the art at the time of the invention would predict

(or reasonably expect) that guanidine-denatured IL-4 (or a mutein thereof) would bind to IMAC-resins.

The present specification states, “[a]lthough native Interleukin-4 contains several histidine-residues in α -helical (His(59)-X-X-X-Asp), β -strand (His(1)-X-Cys, His(75)-X-His) and β -turn (His(1)-X-X-Asp) motives, and it was known from the literature that native Interleukin-4 is bound to IMAC (Naveh et al. (1991): US Patent 5,034,133, Schering cooperation[*sic*]) it is surprising that guanidin[e]-denatured Interleukin-4 also binds to IMAC-resins.”

The cited references are consistent with the present specification. WYLLIE does not disclose or even suggest that IMAC may be used for guanidine-denatured IL-4. Moreover, as acknowledge by the Examiner, the remaining references are silent regarding purification of IL-4 by IMAC.

For at least the foregoing reason, the Applicant respectfully requests that the §103(a) rejections of the claims be reconsidered and withdrawn.

4. Conclusion

Favorable reconsideration of this application is respectfully requested.

Respectfully submitted,

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